REMARKS

Claim Status and Issue of Withdrawn Claims

Claims 48, 49, and 51-146 are pending in this application. Of these, Claims 48 and 49 have been withdrawn from consideration and Claims 76, 113, and 138 amended herein to remove the language "to inhibit oxidation."

Double Patenting

Claims 51-53, 55-68, 70-89, 91-104, and 106-123 are rejected on the grounds of nonstatutory obviousness-type double patenting ("ODP") over claims 1-6 of U.S. Patent #6,645,463. Applicants shall file a terminal disclaimer in compliance with 37 CFR 1.321(c) once the claims of the present application are indicated as allowable but for the double patenting issue set forth herein.

Rejection under 35 U.S.C. §112, 1st ¶

Claims 76, 77, 113, and 114 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement commensurate with the claim scope based on Examiner's interpretation of the phrase "to prevent oxidation." Without commenting on the propriety of the rejection, it is Applicants' belief that the present rejection is obviated by the foregoing claim amendments, removing the language "to inhibit oxidation" from Claims 76, 113 as well as Claim 138. Withdrawal of the rejection is therefore respectfully requested.

Rejection under 35 U.S.C. §103

Claims 51-82 and 84-146 are rejected under 35 U.S.C. §103(a) as being obvious over Modi (USPN 6,214,375) in view of Wheeler et al. Applicants respectfully traverse this rejection for the following reasons. In the Office Action dated August 27th, 2007, Examiner alleged that it would have obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of Modi and incorporate a radiopharmaceutical into the emulsion to arrive at the present invention. While Applicants concede that Wheeler et al. discloses the use of [^{14}C]triolein as a radioactive marker, those of ordinary skill in the art would have no motivation for combining the references in the manner suggested by the Examiner. In the post-KSR landscape, it remains improper to combine references

where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983).

The present invention is directed to a surface-modified lipoprotein-like oil-in-water emulsion that demonstrates stability and remains intact in circulation, making its use particularly desirable in the imaging context. In fact, one of the major problems the present invention seeks to avoid is the loss of contrast agent from the delivery vehicle, the same problem which has plagued the use of liposomal delivery vehicles in the art. It should be emphasized therefore that Modi teaches the use of liposomes as carriers for medicinally active agents. Liposomes are recognized by ordinarily skilled artisans as being distinct from oil-in-water emulsions in principle, structure, mechanism of action, and method of production. At the most basic level, liposomes comprise one or several lipid ***double*** layers with an ***aqueous inner space***. *See* lines 11-20, pg. 2 of the instant speicfication. In contrast, our invention is characterized by a ***lipophilic core*** surrounded by ***a monolayer*** of polar lipids. The difference in structure culminates in different pharmaceutical properties. Liposomes are generally known to be less stable and having a lower lipophilic drug loading capacity as such compounds are necessarily relegated to the lipid bilayers. These and other disadvantages were noted in the instant specification at lines 20-26, pg. 3, reproduced below, and are some of the problems in the art that the claimed invention was intended to overcome.

Investigators have attempted to load liposomes with both ionic and non-ionic water-soluble urographic or hepatobiliary contrast agents, or to incorporate brominated phosphatidylcholine into the bilayer membrane. However, stabilization of the resulting liposome against loss of contrast media from the bilayers has proven to be a major problem. Moreover, incorporation of neutral lipophilic agents into the bilayer is limited by the low solubility of the lipophilic agents in the membrane matrix and the restricted loading capacity of the liposome.

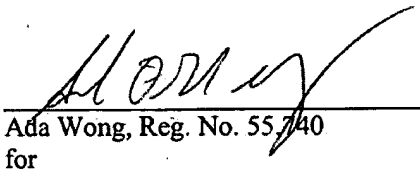
Contrary to the emulsions of the present invention, Modi's liposomes were designed to achieve a depot effect, *i.e.* progressive release of the medicinally active agent from the liposomes into the chosen site. While such release is critical for the delivery of the medicinally active agents in Modi, it defeats the purpose of the present invention. The lipophilic agent of the present invention is situated at the lipophilic core so as to keep it in place, permitting the structure as a whole to maintain stability over time. Those of ordinary skill in the art, given their awareness of the problems associated therein, would be discouraged from incorporating a contrast agent within Modi's liposomes. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Should the Examiner have any continuing objections, the Applicants respectfully ask the Examiner to contact the undersigned at 415-442-1490 (direct line) in order to expedite allowance of the case. Authorization is granted to charge any outstanding fees due at this time for the continued prosecution of this matter to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 (matter no. 066254-5003-US01).

Respectfully submitted,

Date: February 27, 2008 By: 

Ada Wong, Reg. No. 55,740
for
Jeffry S. Mann, Reg. No. 42,837
MORGAN, LEWIS & BOCKIUS LLP
2 Palo Alto Square
3000 El Camino Real, Suite 700
Palo Alto, CA 94306
(415) 442-1490